



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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NOV - 2 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: XRM-4725 HERBICIDE FORMULATION
DERMAL SENSITIZATION STUDY - GUINEA PIGS

TO: CLARE GRUBBS
PRODUCT MANAGER (74)
REGISTRATION DIVISION (H7505C)

FROM: LINDA L. TAYLOR, PH.D. *Linda Lee Taylor* 10/20/89
TOXICOLOGY BRANCH II, SECTION II
HEALTH EFFECTS DIVISION (H7509C)

THRU: K. CLARK SWENTZEL *K. Clark Swentzel* 10/23/89
SECTION II HEAD, TOXICOLOGY BRANCH II
HEALTH EFFECTS DIVISION (H7509C)

AND

MARCIA VAN GEMERT, PH.D. *M. van Gemert* 10/27/89
CHIEF, TOXICOLOGY BRANCH/HFAS/HEB (H7509C)

REGISTRANT: DOW CHEMICAL U.S.A.
CHEMICAL: 2,4-D ISOPROPYLAMINE
SYNONYM: XRM-4725 HERBICIDE FORMULATION
PROJECT: 9-2275
CASWELL No.: 315
RECORD No.: 252179
IDENTIFYING No.: 0073
PRD No.: 412337-01
ACTION REQUESTED: NONE SPECIFIED; STUDY REPORT SUBMITTED FOR REVIEW.

COMMENT: IN RESPONSE TO THE REREGISTRATION OF 2,4-D, A DERMAL SENSITIZATION STUDY WAS SUBMITTED ON XRM-4725 FORMULATION, WHICH CONTAINS 39.3% OF THE ACTIVE INGREDIENT (2,4-D ISOPROPYLAMINE SALT).

UNDER THE CONDITIONS OF THE STUDY, UNDILUTED XRM-4725 (39.3% 2,4-D ISOPROPYLAMINE SALT) WAS NOT SHOWN TO BE A SKIN SENSITIZER. THE STUDY IS CLASSIFIED AS CORE MINIMUM.

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REVIEWED BY: LINDA L. TAYLOR, PH.D.
SECTION II, TOX. BRANCH II (H7509C)
SECONDARY REVIEWER: K. CLARK SWENTZEL
HEAD SECTION II, TOX. BRANCH II (H7509C)

Linda Lee Taylor 10/20/89
K. Clark Swentzel 10/20/89

DATA EVALUATION REPORT

STUDY TYPE: DELAYED CONTACT HYPERSENSITIVITY
GUINEA PIGS

TOX CHEM NO: 315

MRID NO: 412337-01

TEST MATERIAL: XRM-4725 HERBICIDE FORMULATION

SYNONYMS: 2,4-D ISOPROPYLAMINE SALT

STUDY NUMBER: HET M-004725-003

SPONSOR: DOW CHEMICAL U.S.A.

TESTING FACILITY: DOW CHEMICAL U.S.A. MAMMALIAN AND ENVIRONMENTAL
TOXICOLOGY/HEALTH AND ENVIRONMENTAL SCIENCES

TITLE OF REPORT: XRM-4725 HERBICIDE FORMULATION: DERMAL SENSITIZATION
POTENTIAL IN THE GUINEA PIG

AUTHORS: R.E. CARREON AND J.M. WALL

REPORT ISSUED: DECEMBER 12, 1984

CONCLUSIONS: UNDER THE CONDITIONS OF THE STUDY, UNDILUTED XRM-4725
(39.3% 2,4-D ISOPROPYLAMINE SALT) WAS NOT SHOWN TO BE A SKIN SENSITIZER.

CLASSIFICATION: CORE MINIMUM.

A. MATERIALS:

1. TEST COMPOUND: XRM-4725 HERBICIDE FORMULATION
DESCRIPTION: AMBER LIQUID
BATCH #: IDENTIFIED AS GHD-1087-65
PURITY: A-I. 39.3% ± 0.1% (2,4-D ISOPROPYLAMINE)
2. TEST ANIMALS:
SPECIES: GUINEA PIGS (MALES)
STRAIN: HARTLEY ALBINO
AGE: NOT SPECIFIED
WEIGHT: 250-300 g
SOURCE: CHARLES RIVER BREEDING LABORATORIES, INC.

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STUDY DESIGN: THE METHOD USED IS THAT DESCRIBED IN THE EPA GUIDELINES, 1982 (MODIFICATION OF THE MAGUIRE METHOD 1973), AS DESCRIBED IN J. Soc. COSMETICS CHEM. 24, 151-162 (1973). BODY WEIGHTS WERE OBTAINED FOR EACH ANIMAL PRIOR TO TREATMENT, AND ON DAYS 7, 14, 21, AND 28.

THE ANIMALS WERE RANDOMLY ASSIGNED TO THEIR GROUPS. THE HAIR ON THE BACK OF EACH ANIMAL WAS CLIPPED FREE OF HAIR 48 HOURS PRIOR TO DERMAL APPLICATION. TEN GUINEA PIGS RECEIVED 4 APPLICATIONS OF THE UNDILUTED TEST MATERIAL WITHIN 6 DAYS DURING THE INSULT PHASE OF TESTING. NINE OTHER GUINEA PIGS (THE TENTH WAS SACRIFICED AFTER 24-HOURS OF EXPOSURE TO THE POSITIVE CONTROL FOR HUMANE REASONS) RECEIVED DER 331 EPOXY RESIN AS A 10% SOLUTION IN DOWANOL DPM/TWEEN 80, WHICH IS A KNOWN SKIN SENSITIZER (POSITIVE CONTROL). EACH INSULT APPLICATION CONSISTED OF 0.1 ML OF TEST MATERIAL OR POSITIVE CONTROL RESIN APPLIED TO A 15 MM X 15 MM GAUZE SQUARE PATCH, PLACED ON THE BACK OF THE GUINEA PIG, THEN SECURED AND COVERED WITH ADHESIVE TAPE. THE FIRST INSULT APPLICATION WAS ALLOWED TO REMAIN IN PLACE FOR 24 HOURS, THEN REMOVED, AND A SECOND 0.1 ML APPLICATION WAS MADE. AT THE THIRD APPLICATION, 0.2 ML OF FREUND'S ADJUVANT WAS INJECTED INTRADERMALLY ADJACENT TO THE INSULT SITE. AFTER 48 HOURS, THE PATCH WAS REMOVED AND A FRESH PATCH OF 0.1 ML OF THE MATERIAL WAS APPLIED. THE LAST PATCH WAS REMOVED 48 HOURS LATER AND THE ANIMALS WERE ALLOWED TO REST FOR TWO WEEKS (INDUCTION PERIOD). OBSERVATIONS FOR PRIMARY IRRITATION EFFECTS WERE MADE AND RECORDED EACH TIME THE PATCHES WERE REMOVED.

CHALLENGE PHASE - BOTH FLANKS OF EACH ANIMAL WERE CLIPPED AND CHALLENGED WITH THE TEST MATERIAL/POSITIVE CONTROL (SAME DOSAGES AS IN INSULT PHASE) TWO WEEKS AFTER THE LAST APPLICATION. THE CHALLENGE APPLICATIONS WERE NOT COVERED. THE SKIN RESPONSE WAS RECORDED AT 24 AND 48 HOURS.

RESULTS: NONE OF THE ANIMALS CHALLENGED WITH THE UNDILUTED TEST MATERIAL DISPLAYED ANY SIGNS OF REDNESS. THE POSITIVE CONTROL ANIMALS (8 OUT OF 9) DISPLAYED SLIGHT TO MARKED REDNESS. NO EDEMA WAS OBSERVED IN ANY OF THE ANIMALS.

CONCLUSION

UNDER THE CONDITIONS OF THE STUDY, XRM-4725 WAS NOT SHOWN TO BE A SKIN SENSITIZER. THE STUDY IS CLASSIFIED AS CORE MINIMUM.

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